

## REMARKS

### **Status of the Claims**

The following claims are now pending in the application: Claims 1, 3-5, and 17-24.

Claims 1, 5 and 22-24 are amended. No change in scope or meaning of these claims results from this amendment.

No new matter is introduced.

### **The Rejection Under 35 U.S.C. § 112**

Claims 1, 3-5, and 17-24 are rejected under 35 U.S.C. § 112, first paragraph, as failing to enable one of skill in the art to make and use the invention. Respectfully, this rejection is traversed.

In the present Office Action, the U.S. Patent and Trademark Office (PTO) acknowledges Applicant's IDS, filed 3/29/05 and 5/13/02. Office Action, page 2, item 4. Applicant notes that the relevant IDSs were filed not on the dates recited above but on March 24, 2005 and April 26, 2002, respectively. Further, the PTO refers to Applicant's previous amendment and arguments as having been filed on "3/4/05". Office Action, page 2, items 1 and 3, and item 6, paragraph 2. Applicant notes that the relevant previous amendment is found not on the date recited above but on February 28, 2005. Further, the PTO states, "... for the same reasons set forth in the previous Office Action mailed 11/30/04". Office Action, page 2, item 6, paragraph 1, last line; emphasis added. Applicant notes that the relevant previous Office Action is found not on the date recited above but on November 29, 2004.

According to the PTO, the specification is "enabling for a method for detecting a compound that affects (Smooth Muscle Cell) SMC proliferation ..." Office Action, page 2, item 6, lines 2-3. The PTO, however, states:

... [the specification] does not reasonably provide enablement for a method for detecting compounds that affect any "cell proliferation" comprising adding a compound having unknown cellular proliferative activity to a first cell culture; measuring the amount of HSPG in the first cell culture, and comparing the amount of HSPG in the first cell culture to the amount of any HSPG in a second cell culture

not treated with the compound in claim 1, wherein the HSPG is syndecan or glypican in claims 3 and 23-24, wherein the first cell culture and second cell culture are grown in serum-free media in claim 21. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 11/[29]/04. Office Action, page 2, item 6, lines 6-15; emphasis added.

In particular, the PTO states:

a) **PTO:** “[the specification] does not reasonably provide enablement for a method ... wherein the first cell culture and second cell culture are grown in serum-free media ... for reasons set forth in the previous Office Action mailed 11/[29]/04.” Office Action, page 2, item 6, first paragraph, lines 11-12; emphasis added.

In the previous Office Action, the PTO cites Ettenson *et al.* to support the contention that there is lack of enablement for growth in serum-free media. Previous Office Action dated November 29, 2004, page 4, first full paragraph. In particular, the PTO states,

... the claims do not require the presence of conditioned media in the claimed methods, however, Ettenson *et al.* (J Cell Physiol. 2000 Jul; 184(1):93-100) teach that endothelial heparin sulfate is necessary but not sufficient for control of vascular smooth muscle cell growth ... Therefore, it is unclear how the compound would affect the cell proliferation in the absence of the conditioned media.” Previous Office Action dated November 29, 2004, page 4, first full paragraph; emphasis added.

Applicant points out that the term “conditioned media”, as used by Ettenson *et al.*, does not require the presence of serum. Conditioned media, as that term is used by Ettenson *et al.*, refers to media that is exposed to cells for a period of time. In fact, Ettenson *et al.*’s conditioned media is actually prepared under serum-free conditions because “the [endothelial] cells were then washed and incubated for 30 min in serum-free DMEM at 37°C, followed by a 24-h incubation in serum-free DMEM ...”, followed by centrifugation of the medium to remove cells and debris. Ettenson *et al.*, page 94, Materials and Methods, lines 26-39. Further, regarding the presently claimed methods comprising measuring an amount of HSPG, Applicant has shown that HSPG can be measured under serum-free conditions. Application, Figure 1B, see “serum-free” bar.

There is thus adequate teaching in the specification for those of skill in the art to make and/or use the invention commensurate in scope with the claims.

Withdrawal of the present rejection is respectfully requested.

b) **PTO:** “While applicant asserts that Vascular SMCs express syndecans 1, 2 and 4, glypican-1 and perlecan, yet claiming a method for detecting a compound that affects any “cell” proliferation. Applicant has not address[ed] the issue of what type of cells produce syndecan, glypican or perlecan other than SMC.” Office Action, page 2, third paragraph of Item 6.

Applicant at least discloses that, other than SMCs, HSPG is expressed by endothelial cells (specification, page 5, line 21). Further, the references relied on by the PTO, and already of record in the present Application, disclose that HSPGs are expressed in a variety of cells including endothelial cells, smooth muscle cells, fibroblasts, Chinese hamster ovary cells, and macrophages. See, for example, Paka *et al.* (abstract Nov. 2, 1999) abstract, line 1 (endothelial cells); Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22) paper, Figure 1A (smooth muscle cells); Obunike *et al.* paper, Figures 1 and 6 (fibroblasts, Chinese hamster ovary cells (CHO cells), and macrophages). At the time of the invention, it was known to the skilled artisan that HSPG is expressed in various cell types. Applicant further points out that the cells used to detect a compound can, but need not, be of the same type as the cells whose proliferation is affected by the compound.

There is thus adequate teaching in the specification for those of skill in the art to make and/or use the invention commensurate in scope with the claims.

Withdrawal of the present rejection is respectfully requested.

c) **PTO:** “Applicant argues that one of skill in the art would understand that a similar process of immunoprecipitation [] could be used for the measurement of syndecan and glypican. However, the specification fails to provide an antibody that binds either syndecan or glypican and immunoprecipitate[s] them. In the absen[ce] of such antibodies the skilled artisan would not be able to measure the syndecan or glypican nor discriminate between perlecan, syndecan, or glypican when measuring the amount of HSPGs.” Office Action, page 2-3, Fourth paragraph of Item 6.

For reasons that follow, Applicant respectfully disagrees with PTO’s contention that in the absence of antibodies the skilled artisan would not be able to measure the syndecan or glypican nor discriminate between perlecan, syndecan, or glypican when measuring the amount of HSPGs.

First, Applicant continues to hold that the specification is enabling for measuring the amount of a HSPG using antibodies as previously stated, for reasons of record. Further, Applicant maintains that one skilled in the art can without undue experimentation measure the amount of HSPG without a need for antibodies.

As demonstrated by Applicant's disclosure as well as by the references relied upon by the PTO and already of record, the amount of HSPG in a cell can at least be measured by, for example, a procedure involving (<sup>35</sup>S)sulfate radiolabel and DEAE-cellulose chromatography. See, for example, Specification, page 12, Example I; Paka *et al.* (abstract Nov. 2, 1999), Abstract, line 4; Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), page 36404, first column, Materials and Methods, lines 5-30; Obunike *et al.*, page 112, columns 1-2, Methods section.

Further, without using antibodies, the skilled artisan would be able to measure perlecan, syndecan or glypican or discriminate between perlecan, syndecan, or glypican at least by measuring the amount of their respective ribonucleic acids such as, for example, their respective mRNA. See, for example, Specification, page 4, lines 13-16; Paka *et al.* (abstract Nov. 2, 1999), Abstract, lines 12-13; Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), page 36404, first column, Materials and Methods, lines 39-54.

There is thus adequate teaching in the specification for those of skill in the art to make and/or use the invention commensurate in scope with the claims.

Withdrawal of the present rejection is respectfully requested.

d) **PTO:** "Regarding the molecule[,] applicant argues that a person may use the methods of the present invention to determine the effect of any molecule or compound on cell proliferation. Applicant concludes that the identity of the molecule depends entirely on the inquiry performed by the end user of the invention. However, in order to practice the claimed method the skilled artisan needs to know the chemical and physical properties of the molecule to be screened." Office Action, page 3, lines 5-10.

In order to clarify this rejection and refocus the issue raised by the PTO, Applicant refers to "the reasons set forth in previous Office Action mailed 11/[29]/04". In the previous Office action, the PTO states:

Further at issue **the claimed molecule** of claim 5, the specification does not provide guidance the skilled artisan as to what molecules to be screened. While the

dictionary provides a meaning for the word molecule as the smallest particle of a substance that retains the chemical and physical properties of the substance and is composed of two or more atoms; a group of like or different atoms held together by chemical forces. However, the specification fails to provide such chemical and physical properties of **the claimed molecule**. Previous Office action mailed 11/29/04, page 4, third full paragraph; emphasis added.

It appears that Applicant and the PTO differ on what is being presently claimed. Applicant respectfully asserts that the claimed invention is to a method for detecting a compound that affects cell proliferation and not the actual compound itself. Accordingly, Applicant believes that this rejection is improper as to a claimed method and cannot therefore be sustained, and withdrawal of the present ground of rejection is respectfully requested.

There is thus adequate teaching in the specification for those of skill in the art to make and/or use the invention commensurate in scope with the claims.

Withdrawal of the present rejection is respectfully requested in light of the remarks above.

#### **The Rejection Under 35 U.S.C. § 102(b)**

Claims 1, 3-5, 17, 19 and 22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Paka *et al.* (abstract Nov. 2, 1999). Respectfully, this rejection is traversed.

The PTO maintains the rejection “for the same reasons set forth in the previous Office Action mailed 11/[29]/04.” Office Action, page 3, item 8. Further, according to the PTO, “there is no objective evidence of record that show[s] whether the asserted claimed HSPGs inhibit or do not inhibit cell proliferation. Therefore, it is clear that both Paka *et al.* [(abstract Nov. 2, 1999)] and applicant add the same compound to the same cells to achieve the same screening results by measuring the amount [of] HSPG ... nor does applicant provide objective evidence to distinguish the prior art from the claimed invention.” Office Action, page 4, lines 13-18.

In the preceding phrase above, Applicant believes the PTO intended to refer to compounds instead of HSPGs, (*i.e.*, according to the PTO, “there is no objective evidence of record that show[s] whether the asserted claimed [compounds] inhibit or do not inhibit cell proliferation.”) If Applicant’s understanding is incorrect, Applicant would appreciate



clarification on this point. Regardless, Applicant respectfully disagrees with the contention that Paka *et al.* (abstract Nov. 2, 1999) anticipates the present claims.

A fair reading of Paka *et al.* (abstract Nov. 2, 1999) suggests to the skilled artisan that the reference determines that apoE affects cell proliferation by 1) adding apoE to cells, 2) measuring the amount of [<sup>3</sup>H]thymidine incorporation into DNA of the cells, and 3) comparing the amount of [<sup>3</sup>H]thymidine incorporation in the cells to the amount of [<sup>3</sup>H]thymidine incorporation in cells not treated with apoE. Paka *et al.* (abstract Nov. 2, 1999), abstract, lines 7-9. Thus, according to Paka *et al.* (abstract Nov. 2, 1999), a decrease in [<sup>3</sup>H]thymidine incorporation into DNA indicates that apoE affects cell proliferation by inhibiting it (*i.e.*, an antiproliferative effect). And apoE, according to Paka *et al.* (abstract Nov. 2, 1999), is a compound having known cellular proliferative activity. Paka *et al.* (abstract Nov. 2, 1999), abstract, line 3-4 (“in this study we determined whether the antiproliferative effect of apoE is due to increased HS production.”)

Paka *et al.* (abstract Nov. 2, 1999) does not detect a compound that affects cell proliferation either by adding a compound having unknown cell proliferative activity or by measuring and comparing the amount of HSPG to indicate cell proliferation. Accordingly, Paka *et al.* (abstract Nov. 2, 1999) cannot anticipate the present claims.

Further, objective evidence of record that shows whether the asserted claimed [compounds] inhibit or do not inhibit cell proliferation is found at least in the Examples section of the present application. As shown in Example VI on pages 16-17 of the application, Applicant screens test compounds 1-7 for their effect on HSPG (*i.e.*, perlecan) expression. With only seven compounds tested, Applicant is successful in discovering a compound that inhibits perlecan production, a compound that stimulates perlecan production, and five other compounds that show no effect. Application, page 17, lines 5-8. Applicant further shows that one of the discovered compounds, namely RUS 3108, affects cell proliferation in an animal. Specification, page 17, lines 12-15. As shown in Example VIII, RUS 3108 reduces cell proliferation caused by balloon catheter-induced injury of the carotid artery of an animal (*i.e.*, reduces neointimal formation following vessel injury). See Application, page 19 Table 1.

Accordingly, Paka *et al.* (abstract Nov. 2, 1999) does not teach or suggest the claimed invention. Withdrawal of the present rejection is respectfully requested in light of the remarks above.

**The Rejection Under 35 U.S.C. § 102(b)**

Claims 1, 3-5, 17, 19-20 and 22-23 are rejected under 35 U.S.C. § 102(b) as being anticipated by Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22). Respectfully, this rejection is traversed.

The PTO maintains the rejection “for the same reasons set forth in the previous Office Action mailed 11/[29]/04.” Office Action, page 4, item 9.

Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22) determines apoE affects cell proliferation by 1) adding apoE to cells, 2) measuring the amount of **cells** or **[<sup>3</sup>H]thymidine incorporation into DNA** of the cells, and 3) comparing the amount of cells or [<sup>3</sup>H]thymidine incorporation in the cells to the amount of cells or [<sup>3</sup>H]thymidine incorporation in cells not treated with apoE. See, for example, Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), page 36404, Materials and Methods section, first column, lines 31-38. Thus, according to Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), **a decrease in cell number or [<sup>3</sup>H]thymidine incorporation into DNA** would indicate that apoE affects cell proliferation (*i.e.*, an antiproliferative effect). And apoE, according to Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), is a compound having **known** cellular proliferative activity. Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), abstract, line 1.

Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22) does not teach or suggest detecting a compound that affects cell proliferation by adding a compound having **unknown** cell proliferative activity nor by **measuring and comparing the amount of HSPG** to indicate cell proliferation. Accordingly, Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22) cannot anticipate or suggest the present claims.

Withdrawal of the present rejection is respectfully requested in light of the remarks above.

**The Rejection Under 35 U.S.C. § 102(b)**

Claims 1, 3-5, 17, 19-20 and 22 are rejected under 35 U.S.C. § 102(b) as being anticipated by Obunike *et al.*. Respectfully, this rejection is traversed.

The PTO maintains the rejection “for the same reasons set forth in the previous Office Action mailed 11/[29]/04.” Office Action, page 5, item 10.

Obunike *et al.* discloses that cell lines genetically modified to endogenously express apoE or LPL have increased production of proteoglycans. Obunike *et al.* does not teach or suggest detecting a compound that affects cell proliferation by adding a compound and measuring the amount of HSPG. In fact, according to Obunike *et al.*, adding a compound does not even affect proteoglycan levels. “[A]ddition of neither apoE nor anti-human apoE antibody altered PG production in the medium, pericellular pool, and intracellular pool.” Obunike *et al.*, page 115, first column, last paragraph sixth sentence; emphasis added; See also abstract, page 111, lines 13-14. Likewise, addition of LPL also did not affect PG metabolism. Obunike *et al.*, page 115, second column, last paragraph preceding Discussion section. Accordingly, Obunike *et al.* cannot anticipate the present claims, at least because Obunike *et al.* does not “add” a compound to cells.

Further, to establish a *prima facie* case of anticipation a general level of operability is required. MPEP §2121.

*Prima facie* anticipation in the present case is further negated by inoperability of the Obunike *et al.* reference as it relates to ineffectiveness of an added agent to affect the amount of HSPG. According to Obunike *et al.*, “addition of neither apoE nor anti-human apoE antibody altered PG production in the medium, pericellular pool, and intracellular pool.” Obunike *et al.*, page 115, first column, last paragraph sixth sentence; emphasis added; See also abstract, page 111, lines 13-14. Likewise, addition of LPL also did not affect PG metabolism. Obunike *et al.*, abstract, page 111, lines 14-15 and page 115, last paragraph preceding Discussion section. Absent operability of the Obunike *et al.* reference, therefore, a *prima facie* case of anticipation against the claims cannot therefore be sustained, and withdrawal of the present ground of rejection is respectfully requested.

Withdrawal of the present rejection is respectfully requested in light of the remarks above.



**The Rejection Under 35 U.S.C. § 103(a)**

Claims 1, 3, and 23 are rejected under 35 USC 103(a) as being unpatentable over Paka *et al.* (abstract Nov. 2, 1999) or Obunike *et al.* in view of Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22). Respectfully, this rejection is traversed.

The PTO maintains the rejection “for the same reasons set forth in the previous Office Action mailed 11/[29]/04.” Office Action, page 5, item 12.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP §2143. It is well established that failure to meet any one of these criteria negates a finding of *prima facie* obviousness.

*Prima facie* obviousness in the present instance is negated at least by lack of any suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine or modify reference teachings.

Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22) shows apoE affects cell proliferation by 1) adding apoE to cells, 2) measuring the amount of **cells or [<sup>3</sup>H]thymidine incorporation into DNA** of the cells, and 3) comparing the amount of cells or [<sup>3</sup>H]thymidine incorporation in the cells to the amount of cells or [<sup>3</sup>H]thymidine incorporation in cells not treated with apoE. See, for example, Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), page 36404, Materials and Methods section, first column, lines 31-38. Thus, according to Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), **an increase in cell number or [<sup>3</sup>H]thymidine incorporation into DNA** indicates that apoE affects cell proliferation.

Not only does Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22) at least lack suggestion or motivation to modify its teaching to measure the amount of HSPG instead of cells or [<sup>3</sup>H]thymidine incorporation, the reference appears to teach away from such a modification. For example, the reference states, “apoE increased HSPG production in endothelial cells.” Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), page 36403, second column, lines 24-25. Yet, despite such increase, “[a]poE did not inhibit proliferation of endothelial cells.” Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), page 36403, abstract lines 19-20. Also, “[i]n certain cell types ... blocking perlecan production via antisense DNA inhibited cell growth.” Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), page 36407, column 1, lines 20-22. Further, “[a]lthough *in vitro* all isolated HSPGs are effective inhibitors of SMC proliferation, the identity of the antiproliferative

HSPGs *in vivo* is not known. Cell surface HSPGs are required for the mitogenic activity of several growth factors ... and thus are unlikely to inhibit cell growth.” Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), page 36407, column 1, lines 7-12.

Paka *et al.* (abstract Nov. 2, 1999) shows apoE affects cell proliferation by 1) adding apoE to cells, 2) measuring the amount of [<sup>3</sup>H]thymidine incorporation into DNA of the cells, and 3) comparing the amount of [<sup>3</sup>H]thymidine incorporation in the cells to the amount of [<sup>3</sup>H]thymidine incorporation in cells not treated with apoE. Paka *et al.* (abstract Nov. 2, 1999), abstract, lines 7-9. According to Paka *et al.* (abstract Nov. 2, 1999), **an increase in [<sup>3</sup>H]thymidine incorporation into DNA** indicates that apoE affects cell proliferation.

Not only does Paka *et al.* (abstract Nov. 2, 1999) at least lack suggestion or motivation to modify its teaching by measuring the amount of HSPG instead of [<sup>3</sup>H]thymidine incorporation, Paka *et al.* (abstract Nov. 2, 1999) teaches away from such a modification. For example, Paka *et al.* (abstract Nov. 2, 1999) states, “[w]e recently showed that apoE stimulates endothelial [cell] production of heparin sulfate (HS) ...” Paka *et al.* (abstract Nov. 2, 1999), abstract, lines 1-2. Yet, despite such a stimulation, “[a]poE did not inhibit proliferation of endothelial cells.” Paka *et al.* (abstract Nov. 2, 1999) abstract, lines 10-11.

Obunike *et al.* discloses that cell lines genetically modified to endogenously express apoE or LPL have increased production of proteoglycans. Obunike *et al.* does not teach or suggest detecting a compound that affects cell proliferation by measuring the amount of HSPG. Further, according to Obunike *et al.*, apoE or LPL exogenously added to cells does not even affect PG production in the cells. “[A]ddition of neither apoE nor anti-human apoE antibody altered PG production in the medium, pericellular pool, and intracellular pool.” Obunike *et al.*, page 115, first column, last paragraph sixth sentence; emphasis added; See also abstract, page 111, lines 13-14. Likewise, addition of LPL also did not affect PG metabolism. Obunike *et al.*, abstract, page 111, lines 14-15 and page 115, last paragraph preceding Discussion section. Obunike *et al.*, therefore, does not teach or suggest detecting a compound that affects cell proliferation by measuring the amount of HSPG, nor does the reference provide suggestion or motivation to modify its teaching.

Absent any suggestion or motivation to combine or modify the Paka *et al.* (abstract Nov. 2, 1999), Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), and Obunike *et al.* references, a *prima*

*facie* case of obviousness against the claims cannot therefore be sustained, and withdrawal of the present ground of rejection is respectfully requested.

**The Rejection Under 35 U.S.C. § 103(a)**

Claims 1, 3, and 24 are rejected under 35 USC 103(a) as being unpatentable over Paka *et al.* (abstract Nov. 2, 1999) or Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22) or Obunike *et al.* in view of U.S. Patent No. 6,306,613 ('613) to Flowrkiewicz *et al.* Respectfully, this rejection is traversed.

The PTO maintains the rejection "for the same reasons set forth in the previous Office Action mailed 11/[29]/04." Office Action, page 6, item 13. Further, Applicant thanks the PTO for pointing out '613s filing date, which Applicant inadvertently misstated without deceptive intent in the previous response.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP §2143. It is well established that failure to meet any one of these criteria negates a finding of *prima facie* obviousness.

*Prima facie* obviousness in the present instance is negated at least by lack of any suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine or modify reference teachings.

Applicant restates the discussion above as it relates to Paka *et al.* (abstract Nov. 2, 1999), Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), and Obunike *et al.* references.

'613 discloses methods for identifying and using modulators of leaderless protein export. See '613, U.S. Patent No. 6,306,613, Title. According to '613, modulation of export can be achieved by altering binding of the leaderless protein and a transport molecule such as glypican. '613, U.S. Patent No. 6,306,613, Abstract, lines 1-12; See also column 15, lines 18-35. Nowhere, however, does '613 either disclose or suggest the use of HSPG, or specifically glypican, in a method for detecting a compound that affects cell proliferation by measuring the amount of HSPG in cells exposed to the compound. '613 does not even disclose any general discussion. There is no motivation, either express or implied, to modify '613 or combine it with Paka *et al.* (abstract Nov. 2, 1999), Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), or Obunike *et al.* reference to arrive at the present claims.

Response to Office Action of May 12, 2005  
Serial No. 10/091,357

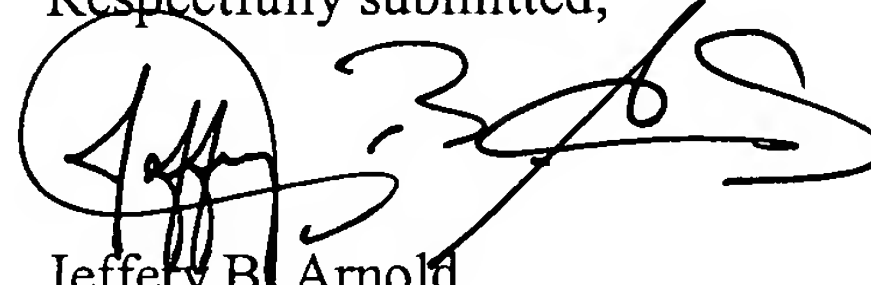
Absent any suggestion or motivation to combine or modify the Paka *et al.* (abstract Nov. 2, 1999), Paka *et al.* (JBC, Dec. 1999, IDS Ref. No. 22), Obunike *et al.* and '613 references, a *prima facie* case of obviousness against the claims cannot therefore be sustained, and withdrawal of the present ground of rejection is respectfully requested.

### CONCLUSION

In view of the foregoing remarks, Applicants respectfully assert that the rejection of the claims as set forth in the final Office Action of May 12, 2005 have been addressed and overcome. Applicants further respectfully assert that all claims are in condition for allowance and request that a Notice of Allowance be issued. If issues may be resolved through PTO's Amendment, or clarified in any manner, a call to the undersigned attorney at (404) 879-2433 is courteously solicited.

The Commissioner is hereby authorized to charge any fees due, or credit any overpayment, to Deposit Account No. 09-0528.

Respectfully submitted,



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